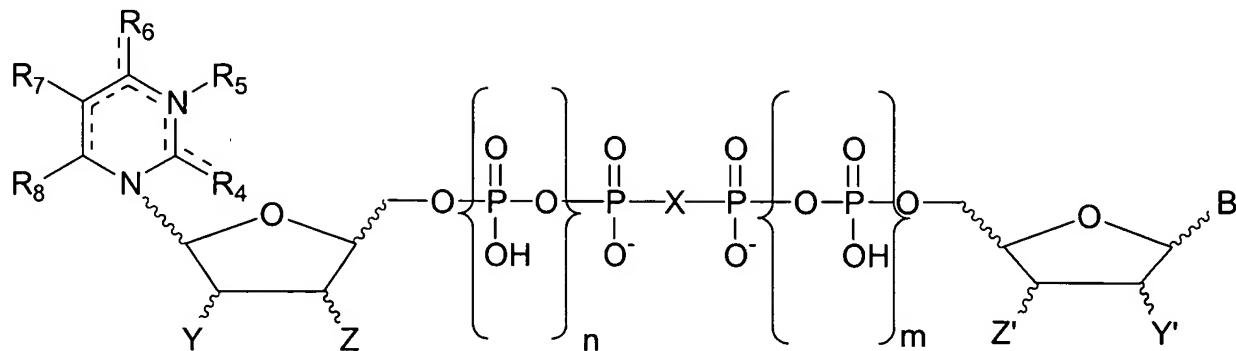


THE AMENDMENT

In the Claims

1. (Currently Amended) A compound of Formula IIIA:

Formula IIIA



wherein:

X is oxygen, methylene, difluoromethylene, imido;

n = 0, 1, or 2;

m = 0, 1, or 2;

n + m = 0, 1, 2, 3, or 4;

B is a purine or a pyrimidine residue linked through the 9- or 1-position, respectively;

Z = OH or N₃;

Z' = OH or N₃;

Y = H or OH;

Y' = H or OH;

provided that when Z is N₃, Y is H or when Z' is N₃, Y' is H;

R₄ is oxo, hydroxy, amino, cyano, aralkoxy, C₁₋₆ alkoxy, C₁₋₆ alkylamino, or dialkylamino;

R₅ is hydrogen, acyl, C₁₋₆ alkyl, phenoxy, C₁₋₅ alkanoyl or

absent;

R_6 is oxo, hydroxy, mercapto, C_{1-4} alkoxy, C_{7-12} arylalkoxy, C_{1-6} alkylthio, amino, C_{1-5} disubstituted amino, triazolyl, C_{1-6} alkylamino or di- C_{1-4} alkylamino, where the alkyl groups is optionally linked to form a heterocycle or link to N^3 to form a substituted ring; or

R_5 and R_6 taken together form a 5-membered fused imidazole ring between positions 3 and 4 of the pyrimidine ring, which is optionally substituted on the 4- or 5- positions of the etheno moiety with C_{1-4} alkyl, phenyl, or phenoxy, which themselves are optionally substituted;

R_7 is hydrogen, hydroxy, cyano, nitro, substituted and unsubstituted C_{2-8} alkenyl, phenyl, substituted and unsubstituted C_{2-8} alkynyl, halogen, CF_3 , substituted and unsubstituted C_{1-6} alkyl, allylamino, bromovinyl, ethyl propenoate, propenoic acid; or

R_6 and R_7 taken together form a 5 or 6-membered saturated or unsaturated ring bonded through N or O at R_6 , such ring optionally contain substituents that themselves contain functionalities;

R_8 is hydrogen, amino or di- C_{1-4} alkylamino, C_{1-4} alkoxy, C_{7-12} arylalkoxy, C_{1-4} alkylthio, C_{7-12} arylalkylthio, carboxamidomethyl, carboxymethyl, methoxy, methylthio, phenoxy or phenylthio; provided that when R_8 is amino or substituted amino, R_7 is hydrogen;

provided that when B = adenine, adenine 1-oxide, or 1, N^6 -ethenoadenine, then:

- (a) $R_6 \neq$ oxo when $R_4 =$ oxo, $Y = Z = OH$ and $R_5 = R_7 = R_8 = H$;
- (b) $R_7 \neq Br$ when $R_4 = R_6 =$ oxo, $Y = Z = OH$, and $R_5 = R_8 = H$;

provided that when B = adenine, then:

- (a) $R_6 \neq$ amino when $R_4 =$ oxo, $Y = Z = OH$, R_5 is absent, $R_7 = R_8 = H$, and $n + m = 0, 1$, or 2;
- (b) $R_7 \neq CH_3$ when $R_4 = R_6 =$ oxo, $Y = H$, $Z = OH$, and $R_5 = R_8 = H$;
- (c) $R_7 \neq F$ when $R_4 = R_6 =$ oxo, $Y = H$, $Z = OH$, $R_5 = R_8 = H$ and $n + m = 2$;

provided that when B = thymine, $Y' = H$ and $Z' = N_3$; then $R_7 \neq F$, when $R_4 = R_6 =$ oxo, $Y = OH$, $Z = OH$, $R_5 = R_8 = H$, and $n + m = 0$;

provided that when B = thymine, Y' = H and Z' = N₃; then R₇ ≠ CH₃ when R₄ = R₆ = oxo, Y = H, Z = N₃, R₅ = R₈ = H, and n + m = 0;

provided that when B = guanine, then:

- (a) R₆ ≠ oxo when R₄ = oxo, Y = Z = OH, R₅ = R₇ = R₈ = H and n + m = 1 or 2;
- (b) R₆ ≠ amino when R₄ = oxo, Y = Z = OH, R₅ is absent, R₇ = R₈ = H, n+m=1 or 2;

provided that when B is uridine, or 5-Br-uridine, then

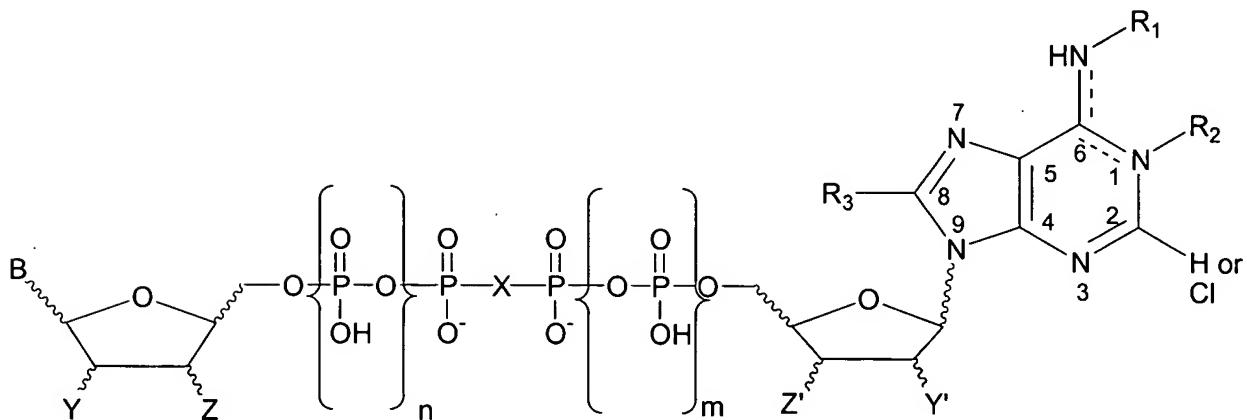
- (a) R₆ ≠ oxo when R₄ = oxo, Y = Z = OH and R₆ = R₇ = R₈ = H;
- (b) R₇ ≠ Br when R₄ = R₆ = oxo, Y = Z = OH, and R₅ = R₈ = H;

provided that when B is 5-FU, then R₇ ≠ F, when R₄ = R₆ = oxo, Y = H, Z = OH, R₅ = R₈ = H, and n + m = 0;

provided that when B is cytosine, then R₆ ≠ amino, when R₄ = oxo, Y = Z = OH, R₅ is absent, R₇ = R₈ = H, and n + m = 1, or 2; and

provided that when B is cytosine, then R₆ ≠ oxo, when R₄ = oxo, Y = Z = OH and R₆ R₅ = R₇ = R₈ = H, and n + m = 2.

2. (Original) A compound according to Formula IIA:



FORMULA IIA

wherein:

X is oxygen, methylene, difluoromethylene, imido;

n = 0, 1, or 2;

m = 0, 1, or 2;

n + m = 0, 1, 2, 3, or 4;

B is a purine residue linked through the 9-position;

Z = OH or N₃;

Z' = OH or N₃;

Y = H or OH;

Y' = H or OH;

provided that when Z is N₃, Y is H or when Z' is N₃, Y' is H;

R₁ is H, C₁₋₈alkyl, phenyl or phenoxy, optionally substituted with halogen, hydroxy, C₁₋₄alkoxy, C₁₋₄alkyl, C₆₋₁₀aryl, carboxy, cyano, nitro, sulfonamido, sulfonate, phosphate, sulfonic acid, amino or substituted amino, wherein the amino is singly or doubly substituted by a C₁₋₄ alkyl and when doubly substituted, the alkyl groups are optionally linked to

form a heterocycle; or A(C₁₋₆alkyl)CONH(C₁₋₆alkyl)B wherein A and B are amino, mercapto, hydroxy or carboxyl;

R₂ is O or is absent; or

R₁ and R₂ taken together forms a 5-membered fused imidazole ring, which is optionally substituted on the 4- or 5- positions of the etheno moiety with C₁₋₄alkyl, phenyl or phenoxy, optionally substituted with halogen, hydroxy, C₁₋₄alkoxy, C₁₋₄alkyl, C₆₋₁₀aryl, arylalkyl, carboxy, cyano, nitro, sulfonamido, sulfonate, phosphate, sulfonic acid, amino or substituted amino, wherein the amino is singly or doubly substituted by a C₁₋₄ alkyl and when doubly substituted, the alkyl groups is optionally linked to form a heterocycle; and

R₃ is H, C₁₋₈alkyl, phenyl or phenoxy, optionally substituted with halogen, hydroxy, C₁₋₄alkoxy, C₁₋₄alkyl, C₆₋₁₀aryl, carboxy, cyano, nitro, sulfonamido, sulfonate, phosphate, sulfonic acid, amino or substituted amino, wherein the amino is singly or doubly substituted by a C₁₋₄ alkyl and when doubly substituted, the alkyl groups is optionally linked to form a heterocycle; C₇₋₁₂arylalkyl; C₁₋₄alkylamino, phenylamino, C₇₋₁₂arylalkylamino, C₁₋₄alkoxy, or C₇₋₁₂arylalkyloxy; C₁₋₄alkylthio, phenylthio, C₇₋₁₂arylalkylthio, or -A(C₁₋₆alkyl)CONH(C₁₋₆alkyl)B- wherein A and B are independently amino, mercapto, hydroxy or carboxyl;

provided that R₁ ≠ H, when X is oxygen, methylene, or difluoromethylene, Y is OH, B is adenine, R₂ is absent, and R₃ is hydrogen;

provided that R₁ ≠ H, when n + m = 2, X is oxygen, Y is OH, B is adenine, R₂ is absent, and R₃ is bromo, or 6-aminohexyl;

provided that R₁ ≠ H, when n + m = 2, X is oxygen, Y is H, B is adenine, R₂ is absent, and R₃ is H;

provided that R₂ ≠ O, when n + m = 2, X is oxygen, Y is OH, R₁ = R₃ = H, and B is adenine, adenine 1-oxide, or 1,N⁶-ethenoadenine;

provided that R₁ and R₂ do not form a 5-membered fused imidazole ring, when n + m = 2, X is oxygen, Y is OH, R₃ is H, and B is adenine, adenine 1-oxide, or ethenoadenine.

3. (Original) The compound according to Claim 1 or 2, wherein the ribosyl moieties are in the D- configuration.

4. (Original) The compound according to Claim 1 or 2, wherein the ribosyl moieties are in the L- configuration.

5. (Previously Presented) A pharmaceutical composition comprising a compound of Formula IIIA or IIA as described in Claim 1 or 2, or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier therefor.

6. (Previously Presented) A method of treating chronic obstructive pulmonary diseases in a mammal by administering an effective chronic obstructive pulmonary disease treatment amount of a compound of Formula IIIA or IIA as described in Claim 1 or 2.

7. (Previously Presented) A method of treating sinusitis, otitis media or nasolacrimal duct obstruction in a mammal by administering an effective mucus secretion clearing amount of a compound of Formula IIIA or IIA as described in Claim 1 or 2.

8. (Previously Presented) A method of treating dry eye in a mammal by administering an effective dry eye treatment amount of a compound of Formula III A or IIA as described in Claim 1 or 2.

9. (Previously Presented) A method of treating retinal detachment in a mammal by administering an effective retinal detachment treatment amount of a compound of Formula IIIA or IIA as described in Claim 1 or 2.

10. (Previously Presented) A method of facilitating sputum induction in a mammal by administering an effective amount of a compound of Formula IIIA or IIA as described in Claim 1 or 2 to facilitate sputum induction.

11. (Previously Presented) A method of facilitating expectoration in a mammal by administering an effective amount of a compound of Formula IIIA or IIA as described in Claim 1 or 2 to facilitating expectoration.

12. (Previously Presented) A method of treating cystic fibrosis in a mammal by administering an effective amount of a compound of Formula IIIA or IIA as described in Claim 1 or 2 to treat cystic fibrosis.

13. (Currently Amended) ~~The method according to Claim 12, wherein said compound is~~ A method of treating cystic fibrosis in a mammal by administering an effective amount of P¹-(2'-deoxycytidine 5')-P⁴-(uridine 5')tetraphosphate.